



The correlation between serum sodium levels and preeclampsia severity in pregnant women; a cross-sectional study

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ABSTRACT

Introduction: Preeclampsia is a significant pregnancy complication characterized by hypertension and proteinuria, potentially leading to severe maternal and fetal morbidity. The pathophysiology of preeclampsia involves endothelial dysfunction, which may influence various biochemical markers, including serum sodium levels.

Objectives: This study aims to elucidate the relationship between serum sodium concentrations and preeclampsia severity.

Patients and Methods: This cross-sectional study was conducted in 2023 on 112 pregnant women diagnosed with preeclampsia at Akbarabadi and Firoozabadi hospitals in Tehran. Participants were categorized into mild/moderate and severe preeclampsia groups based on clinical criteria. Data collection utilized a researcher-designed checklist that included demographic information such as maternal age and body mass index (BMI), as well as clinical details including delivery type, twin status, proteinuria levels, blood pressure, maternal sodium concentrations measured before and up to 48 hours post-delivery, gestational age, and fetal weight. The primary outcome was evaluating the correlation between maternal serum sodium levels and the severity of preeclampsia.

Results: The study involved 112 women with an average age of 29.37 ± 6.33 years, among whom 57 were diagnosed with severe preeclampsia and 55 with mild or moderate cases. The analysis revealed that there was no statistically significant correlation between serum sodium levels and the severity of preeclampsia ($P > 0.05$).

Conclusion: The findings suggest that serum sodium levels may not be a reliable biomarker for assessing the severity of preeclampsia in pregnant women, highlighting the need for further research to explore other potential indicators that could better reflect the condition's severity and inform clinical management strategies.

Implication for health policy/practice/research/medical education:

The findings of this study found that serum sodium levels may not serve as a reliable biomarker for assessing the severity of preeclampsia in pregnant women. Health policies should prioritize the identification and validation of alternative biomarkers that can more accurately reflect the severity of preeclampsia, thereby enhancing risk stratification and management strategies. In clinical practice, physicians should be cautious in relying on serum sodium levels for evaluating preeclampsia severity and instead focus on integrating other established indicators into routine assessments. Furthermore, future research should explore novel biomarkers and mechanisms underlying preeclampsia to improve understanding and treatment options.

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Introduction

Pre-eclampsia is a serious pregnancy complication characterized by new-onset hypertension occurring after

20 weeks of gestation, often accompanied by proteinuria or other signs of maternal organ dysfunction, such as liver or kidney impairment, and fetal growth restriction

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(1,2). This condition affects approximately 3%-5% of pregnancies and is a significant contributor to maternal and neonatal morbidity and mortality, with potential long-term health implications for both mothers and their children (3,4). The diagnosis is typically based on elevated blood pressure alongside the aforementioned complications, although recent guidelines have also recognized cases without proteinuria if other organ dysfunctions are present (4,5). Management primarily involves monitoring and controlling blood pressure, as well as planning for delivery, which remains the only definitive treatment for pre-eclampsia (6).

Factors predicting pre-eclampsia include a combination of maternal characteristics, medical history, and specific biomarkers. Key maternal risk factors consist of chronic hypertension, obesity, nulliparity, advanced maternal age, and a history of pre-eclampsia in previous pregnancies (5,7). Additionally, biochemical markers such as placental growth factor and soluble fms-like tyrosine kinase-1 have shown promise in enhancing prediction models, particularly when combined with mean arterial pressure and uterine artery Doppler studies (7,8).

Maternal serum sodium levels during pregnancy are typically lower than in nonpregnant women, with a normal range of 130–140 mmol/L due to physiological changes such as increased plasma volume and altered osmoregulation. Hyponatremia, defined as serum sodium levels below 130 mmol/L, can occur during pregnancy and is associated with complications such as preeclampsia. Studies have shown that women with preeclampsia often exhibit significantly reduced serum sodium levels compared to normotensive pregnant women, likely due to sodium retention and altered cell membrane sodium transport. Severe hyponatremia (sodium <125 mmol/L) can increase risks for maternal seizures and adverse neonatal outcomes, necessitating careful monitoring and management to prevent complications (9,10). Previous studies showed that approximately 14.6% of women with preeclampsia exhibit hyponatremia, which correlates strongly with severe features of the condition, such as acute kidney injury, fetal growth restriction, and the need for intensive care admission (11,12). In a cohort study, lower sodium levels were linked to adverse pregnancy outcomes (10). Furthermore, severe maternal hyponatremia has been documented to complicate preeclampsia cases, necessitating careful monitoring and management due to its potential to mimic or exacerbate eclamptic symptoms (13,14). Thus, monitoring serum sodium levels in pregnant women diagnosed with preeclampsia could be crucial for identifying those at greater risk for severe complications.

Objectives

The objective of this study is to investigate the correlation between serum sodium levels and the severity of preeclampsia in pregnant women, utilizing a cross-sectional design to analyze maternal serum sodium

concentrations in relation to clinical parameters indicative of preeclampsia severity. By examining the relationship between sodium levels and preeclampsia severity, this study aimed to contribute to the understanding of potential biomarkers for preeclampsia, ultimately enhancing early detection and management strategies for affected patients.

Materials and Methods

Study design and participants

This cross-sectional and analytical study was conducted on pregnant women diagnosed with preeclampsia referred to Akbarabadi and Firoozabadi hospitals in Tehran in 2023, to explore the correlation between serum sodium levels and the severity of preeclampsia in pregnant women. The study included a total of 112 participants, categorized into mild/moderate and severe preeclampsia groups based on clinical criteria.

Inclusion and exclusion criteria

Inclusion criteria consisted of pregnant women diagnosed with preeclampsia after 20 weeks of gestation, aged between 18 and 45 years. Exclusion criteria included women with a history of chronic hypertension before pregnancy, those with significant medical conditions such as diabetes, renal disease, or cardiovascular disorders that could influence serum sodium levels, individuals currently taking medications affecting electrolyte balance, those who have undergone major surgery or experienced significant trauma within the last one year.

Data collection

Data were collected using a researcher-designed checklist composed of two sections. The first section captured demographic details, including maternal age and body mass index (BMI). The second section focused on clinical information, documenting the type of delivery (normal vaginal delivery or cesarean section), twin status, systolic and diastolic blood pressure, severity of preeclampsia (mild/moderate and severe), proteinuria levels and their severity, maternal sodium concentrations measured before and up to 48 hours after delivery, gestational age, and fetal weight.

Criteria for severe preeclampsia

The severity of preeclampsia is determined based on clinical and laboratory findings, including systolic blood pressure of 160 mm Hg or higher or diastolic blood pressure of 110 mm Hg or higher on two occasions at least six hours apart, significant proteinuria (5 grams or more in a 24-hour urine collection or a protein/creatinine ratio of 0.3 or higher), and evidence of end-organ dysfunction. End-organ dysfunction may manifest as renal impairment (serum creatinine above 1.1 mg/dL or doubling of baseline levels), elevated liver enzymes greater than twice the normal limit, severe persistent headaches, visual disturbances, pulmonary edema, or seizures (eclampsia).

Outcomes

The primary outcome of this study is to evaluate the correlation between maternal serum sodium levels and the severity of preeclampsia in pregnant women.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS, IBM Corp, USA), version 27. The Kolmogorov-Smirnov test was performed to assess the normality of quantitative variables. Frequency distributions between groups were compared using the independent T-test for quantitative variables, while chi-square and Fisher's exact tests were applied for qualitative variables. To examine the correlation between serum sodium levels and preeclampsia severity, univariate and multivariate logistic regression analysis were conducted, with odds ratios (ORs) and 95% confidence intervals (CIs) calculated. A *P* value of less than 0.05 was considered statistically significant.

Results

The study included 112 women with a mean age of 29.37 ± 6.33 years, of whom 57 had severe preeclampsia and 55 had mild or moderate cases. The average BMI was above the normal range. Most deliveries were vaginal, while a smaller proportion were cesarean sections. Most participants were carrying singletons, while a minority had twins. The average fetal weight was within the normal range, and the mean gestational age was at term. Regarding proteinuria, a significant number of women did not exhibit this condition, although various levels of proteinuria were recorded among those who did. The maternal sodium (Na) levels were within the normal range both before and

after delivery (Table 1).

The comparative analysis of demographic characteristics and clinical findings based on the severity of preeclampsia revealed that there were no statistically significant differences in the frequency distribution of delivery type, twin status, maternal age, BMI, proteinuria levels, and maternal Na levels before and after delivery between the groups of women with severe and mild to moderate preeclampsia. However, significant differences were noted in gestational age and fetal weight, with mothers experiencing severe preeclampsia having significantly lower fetal age and weight compared to those with mild or moderate preeclampsia (Table 2).

The assessment of the correlation between maternal sodium levels and the severity of preeclampsia utilized univariate logistic regression analysis, which indicated no statistical correlation between these variables. Furthermore, when adjusting for potential confounders such as maternal age, BMI, fetal weight, and gestational age in a multivariate logistic regression model, the results consistently failed to demonstrate any significant correlation. These findings suggest that maternal sodium levels may not be a contributing factor in the severity of preeclampsia (Table 3).

Discussion

In this study, the investigation into the relationship between serum sodium levels and the severity of preeclampsia revealed no significant correlation, suggesting that variations in serum sodium do not directly influence the clinical severity of this condition. We did not find any studies explicitly reporting a lack of correlation between serum sodium levels and the severity of preeclampsia.

Table 1. Demographic characteristics and clinical findings of included women in the study

Variable	Sub-variable	Frequency	Percent
Delivery type	Vaginal	76	67.9
	Cesarean section	36	32.1
Twin Status	Singleton	104	92.9
	Twins	8	7.1
Proteinuria	No	47	42
	1+	14	12.5
	2+	26	23.2
	3+	9	8
	4+	9	8
	WP	7	6.3
Preeclampsia Severity	Severe	57	50.9
	Mild/moderate	55	49.1

Variable	Mean	SD	Min	Max
Maternal age (y)	29.37	6.33	18	43
Maternal BMI (kg/m²)	27.88	5.45	18.88	48
Gestational age (wk)	36.10	2.71	28	41
Fetal weight (g)	2743.04	618.84	1300	4800
Maternal Na before delivery (mEq/L)	139.02	2.37	134	146
Maternal Na after delivery (mEq/L)	139.23	2.01	134	145
Na changes before and after delivery	0.21	2.88	-7	+6

WP, Worsening proteinuria; SD, Standard deviation; Min, Minimum; Max, Maximum; BMI, Body mass index; Na, Sodium.

Table 2. Frequency distribution of demographic and clinical findings according to preeclampsia severity

Variable		Preeclampsia Severity				P value
		Mild/moderate (n = 57)		Severe (n = 55)		
		No.	%	No.	%	
Delivery type	Cesarean section (n = 36)	19	52.8	17	47.2	0.784*
	Vaginal (n = 76)	38	50	38	50	
Twin status	Singleton (n = 104)	54	51.9	50	48.1	0.432*
	Twins (n = 8)	3	37.5	5	62.5	
Proteinuria	No (n = 47)	26	55.3	21	44.7	0.946**
	1+ (n = 14)	6	42.9	8	57.1	
	2+ (n = 26)	12	46.2	14	53.8	
	3+ (n = 9)	4	44.4	5	55.6	
	4+ (n = 9)	5	55.6	4	44.4	
	WP (n = 7)	4	57.1	3	42.9	
Variable		Mean	SD	Mean	SD	P value
Maternal age (year)		29.98	6.76	28.73	5.86	0.297**
Maternal BMI (kg/m²)		27.08	5.37	28.71	5.47	0.114**
Gestational age (wk)		37.28	1.37	34.87	3.18	<0.001**
Fetal weight (g)		3058.51	357.42	2416.09	663.92	<0.001**
Maternal Na before delivery (mEq/L)		138.75	2.25	139.29	2.47	0.233**
Maternal Na after delivery (mEq/L)		139.19	2.02	139.27	1.99	0.834**
Na changes before and after delivery		+0.43	2.49	-0.01	3.25	0.405**

WP, Worsening proteinuria; SD, Standard deviation; Min, Minimum; Max, Maximum; BMI, Body mass index; Na, Sodium.

*Chi-square, **Fishers' exact test, **Independent T-test.

Table 3. The association of serum sodium levels with preeclampsia severity using univariable and multivariable logistic regression

Serum Sodium Levels		OR	P value	95% CI	
				Lower	Upper
Unadjusted	Maternal Na before delivery (mEq/L)	1.10	0.232	0.94	1.29
	Maternal Na after delivery (mEq/L)	1.02	0.832	0.84	1.22
	Na changes before and after delivery	0.94	0.402	0.831	1.07
Adjusted	Maternal Na before delivery (mEq/L)	1.14	0.186	0.93	1.39
	Maternal Na after delivery (mEq/L)	1.07	0.579	0.84	1.36
	Na changes before and after delivery	0.93	0.449	0.78	1.11

OR, Odds ratio; CI, Confidence interval; Na, Sodium.

However, in contrast to our findings, several studies have explored the potential role of serum sodium and other biochemical markers in preeclampsia. For instance, some research has suggested that alterations in sodium levels may contribute to the pathophysiology of preeclampsia, although these studies often focus on broader electrolyte imbalances or associated biomarkers rather than directly correlating sodium levels with disease severity. In a cross-sectional study by Saha et al involving patients diagnosed with preeclampsia, serum sodium levels were measured alongside other biochemical markers, and statistical analysis indicated that while some electrolyte imbalances were noted, serum sodium exhibited a positive association with the severity of preeclampsia as assessed by clinical parameters such as blood pressure and proteinuria (15). In a study by Tabassum et al, a significant positive correlation was found between increased serum sodium concentrations and systolic blood pressure, suggesting that higher sodium levels may contribute to

the hypertensive manifestations observed in preeclampsia (16). Hsu et al reported a rare case in which hyponatremia caused by hypervolemia in a postpartum preeclampsia patient significantly exacerbated her condition, ultimately leading to cardiopulmonary arrest (17). Another case report by Hinkson et al highlighted that severe maternal hyponatremia complicated the clinical course of preeclampsia, illustrating the potential risks associated with electrolyte imbalances in affected patients (18). Meanwhile, the study by Razavi et al, consisting 332 pregnant women diagnosed with preeclampsia found that the majority of those with hyponatremia exhibited severe features of the condition, indicating that hyponatremia was significantly more prevalent among patients experiencing severe preeclampsia compared to those without severe features (19). In a case series study, Morton et al indicated that hyponatremia is associated with the severity of preeclampsia and should be considered a clinical marker for assessing the condition's severity (20). The study by

Remer et al, containing 700 pre-eclampsia patients found that hyponatremia was significantly correlated with severe features of preeclampsia, including HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome and abnormal kidney function. The study suggested that serum sodium levels should be monitored, particularly in patients with severe features, as hyponatremia was more common in this group (12).

In our study the relationship between serum sodium levels and the severity of preeclampsia yielded no significant correlation, suggesting that serum sodium may not be a reliable biomarker for assessing the severity of this condition. These findings imply that while electrolyte disturbances are common in preeclampsia patients, serum sodium levels alone may not serve as reliable indicators for the severity of the disease, thereby highlighting the complexity of biochemical interactions in the pathophysiology of preeclampsia. Previous studies have shown results regarding the role of hyponatremia in preeclampsia, with the majority indicating associations between decreased sodium levels and preeclampsia. This inconsistency highlights the complexity of preeclampsia as a multifactorial disease, where factors such as renal function, fluid balance, and other biochemical markers may play more critical roles than serum sodium alone. Consequently, further research is necessary to explore these relationships comprehensively and to identify more definitive biomarkers that could aid in the management and understanding of preeclampsia.

Conclusion

In conclusion, this study's findings indicate that maternal sodium levels do not correlate with the severity of preeclampsia, as evidenced by both univariate and multivariate logistic regression analyses. The lack of statistical significance suggests that sodium levels may not play a role in the pathophysiology of preeclampsia, challenging the notion that maternal sodium could serve as a reliable biomarker for assessing the condition's severity. These results underscore the importance of exploring other potential biomarkers and clinical indicators that may better reflect the complexities of preeclampsia and inform management strategies for affected pregnant women. Further research is warranted to identify factors that could contribute to the understanding and treatment of this significant pregnancy complication.

Limitations of the study

The study has several limitations. Firstly, the cross-sectional design restricts the ability to establish causality between serum sodium levels and preeclampsia severity, as it captures data at a single point in time rather than throughout the pregnancy. Additionally, the sample size of 112 participants may limit the generalizability of the findings, as a larger and more diverse population could provide more robust data. The reliance on a researcher-

designed checklist for data collection may introduce bias, as it does not undergo extensive validation compared to standardized instruments. Furthermore, the study's focus on two hospitals in Tehran may not account for regional variations in preeclampsia presentation and management, potentially affecting the applicability of results to broader populations.

Authors' contribution

Conceptualization: Roya Biglarifar and Samaneh Saghaian Larijani.

Data curation: Roya Biglarifar.

Formal analysis: Esra Biglari.

Investigation: Roya Biglarifar and Samaneh Saghaian Larijani.

Methodology: Esra Biglari.

Project Management: Roya Biglarifar.

Resources: All authors.

Supervision: Samaneh Saghaian Larijani.

Validation: Roya Biglarifar and Esra Biglari.

Writing-original draft: All authors.

Writing-reviewing and editing: All authors.

Conflicts of interest

The authors declare no conflict of interest.

Ethical issues

The research was conducted in accordance with the principles outlined in the Declaration of Helsinki. This study resulted from the Obstetrics and Gynecology residential thesis of Roya Biglarifar (Thesis#25806), with the Ethical code (IR.IUMS.FMD.REC.1402.183; <https://ethics.research.ac.ir/EthicsProposalView.php?id=362849>), approved by the Iran University of Medical Sciences, Tehran, Iran. Besides, the authors have ultimately observed ethical issues (including plagiarism, data fabrication, and double publication).

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